

REMARKS

1. ***Claim Rejection – 35 U.S.C. § 103(a)***

Claims 1-10, 12, and 13 stand rejected under 35 U.S.C. §103(a) (“Section 103(a)”) as obvious over Moniz, et al. (U.S. Patent No. 5,288,491 issued Feb. 22, 1994) (“Moniz”), in view of Nair et al. (WIPO Publication No. WO 01/015553) (“Nair”) and Wadsworth, et al. (U.S. Patent No. 6,254,913 issued July 3, 2001) (“Wadsworth”). An invention is unpatentable under Section 103(a) “if the differences between the subject matter sought to be patented over the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which the subject matter pertains.” To establish a *prima facie* case of obviousness, three criteria must be met. “First, there must be some suggestion or motivation . . . to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.” MPEP § 2142.

Nair claimed the use of fruit from a specific list, which does not contain *Morinda citrifolia*, to selectively inhibit COX-2. Wadsworth claimed a method of obtaining *Morinda citrifolia* dietary fiber, and teaches that the fiber can be used in nutritional products. Moniz claims a process for turning *Morinda citrifolia* into powder and teaches that in the Caribbean, the leaves are steamed and applied topically for aches, pains, and tendonitis. The present invention claims a method for selectively inhibiting COX-2 to treat pain and inflammation using processed *Morinda citrifolia*. The Examiner indicated that the presently claimed invention is one borne from routine experimentation, utilizing methods to determine dosage that are well known in the art. The Examiner states that the Applicants have “not demonstrated novelty [sic]” because prior art has shown the same composition to be useful for the same general purpose, the precise

dosage of which could be determined by routine experimentation for the purposes of maximizing effectiveness.

There are several arguments that support the patentability of the present invention. First, as a preliminary matter it is critical that the Examiner treat the claimed invention as a whole; it is not appropriate to single out the dosage as the sole inventive component. Viewed as a whole, the presently claimed method is not borne from routine experimentation, utilizing methods to determine dosage that are well known in the art. Second, the prior art does not suggest the combination of the prior art references cited against the present invention. Third, every element claimed in the present invention is not expressly present in the prior art inventions, and specific COX-2 inhibition is not an inherent property of *Morinda citrifolia*. Fourth, selective inhibition of COX-2 is a long felt but unresolved need, which militates towards holding the present invention nonobvious.

Examiner must treat the claimed invention as a whole. In determining the differences between the prior art, and the claims, the question under 35 U.S.C. 103 is not whether the differences themselves would have been obvious, but whether the claimed invention as a whole would have been obvious. *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530 (Fed. Cir. 1983); *Schenck v. Nortron Corp.*, 713 F.2d 782 (Fed. Cir. 1983). It is inappropriate for the Examiner to identify the dosage element as the only inventive element of the present invention, and then subsequently dismiss the methods to determine an appropriate dosage as common to one skilled in the art. Rather, the examiner must evaluate the nonobviousness of the entire invention. The current invention claims a method of treating pain and inflammation comprising the steps of: administering a pre-determined dose of processed *Morinda citrifolia* to a patient two to three times per day; and limiting undesired COX-1 inhibition relative to COX-2 inhibition by varying

the concentration of said dose depending upon the age, weight, general health, diet, and sex of said patient, as well as the time and route of administration, rate of excretion, drug combination, and the severity of the particular disease being treated. As contended below, the current invention as a whole is more than a product of routine experimentation by one skilled in the art; in fact the invention was unexpected and surprising. *Specification*, at 15. Parsing the invention down to the element of dosage, and subsequently dismissing that element as un inventive defies the admonition of *Stratoflex* and *Schenck*. The fact that processed *Morinda citrifolia* products would selectively inhibit COX-2 was not a certainty that depended solely on routine experimentation.

The prior art does not suggest the combination of references cited against the present invention. “Obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination.” *In re John R. Fritch*, 972 F.2d 1260, 1266 (Fed. Cir. 1992). Any such suggestion must be “found in the prior art, and not based on applicant’s disclosure.” *In re Vaeck*, 947 F.2d 488, 493 (Fed. Cir. 1991). Indeed, “[t]he mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggested the desirability of the modification.” *In re Mills*, 916 F.2d 680, 682 (Fed. Cir. 1990); MPEP § 2142. The level of skill in the art cannot be relied upon to provide the suggestion to combine references. *Al-Site Corp. v. VSI Int’l Inc.*, 174 F.3d 1308 (Fed. Cir. 1999). A “clear and particular” showing of the suggestion to combine is required to support an obviousness rejection under Section 103. MPEP § 2142. Thus, to establish a prima facie case of obviousness against the present invention the Examiner must identify a suggestion in the prior art.

For the reasons set forth below, Applicant submits that the prior art fails to clearly and particularly suggest the combination indicated by the Examiner. Thus, Applicant's claims are not obvious in view of the prior art references. In essence the Applicant urges that the combination of the listed references is not a product of a suggestion contained within them, but a product of inappropriate hindsight analysis. "Hindsight reconstruction" cannot be used "to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention." *Ecolchem, Inc. v. S. California Edison Co.*, 227 F.3d 1361, 1371 (Fed. Cir. 2000) (quoting *In re Fine*, 837 F.2d 1071 (Fed. Cir. 1988)). Rather, "the best defense against hindsight-based obviousness analysis is the rigorous application of the requirement for a showing of a teaching or motivation to combine the prior art references." *Id.* "Combining prior art references without evidence of such a suggestion, teaching, or motivation simply takes the inventor's disclosure as a blueprint for piecing together the prior art to defeat patentability-the essence of hindsight." *Id.* (quoting *In re Dembiczak*, 175 F.3d 994 (Fed. Cir. 1999))

First, as a preliminary matter, it is important to note that none of the references cited against the present invention contain an express suggestion to combine the references. If there was a suggestion it could only be implied, and it is the position of the Applicant that there is no implied suggestion to combine. It would not be obvious to one of ordinary skill in the art to combine the teachings of Nair with those of Moniz in order to find methods to further investigate the selective COX-2 inhibition. First, Nair teaches the use of fruit from a specific "consisting" list to selectively inhibit COX-2. Nair teaches a finite and limited list because it is beyond the scope of his disclosure to claim all fruit. Certainly, one would be mistaken to assume that all fruit extracts selectively inhibit COX-2. Additionally, there is no suggestion to combine because, as Applicants' experiments show, *Morinda citrifolia* relieves pain by at least two methods; one

where both COX-2 and COX-1 are inhibited and one where COX-2 is selectively inhibited. The Office has not shown that Nair teaches a method of determining COX-2 selectivity where a fruit extract relieves pain by limiting both COX-2 and COX-1 and by selectively limiting COX-2. Likewise, Nair does not suggest or motivate one skilled in the art to utilize pure noni, such as that disclosed by Moniz and Wadsworth, as an ingredient in the food supplement. Nair, in fact, teaches away from the use of pure noni. Indeed, Nair specifies that for effective maximization of the food supplement's anti-inflammatory effect, an anthocyanin-containing plant must be processed to reduce the anthocyanin to anthocyanidin. It would not be obvious to one skilled in the art to substitute a form of pure noni for an anthocyanin-containing plant that has been processed to isolate the non-naturally occurring anthocyanidin, such as that disclosed by Nair. Thus, Nair cannot stand as a suggestion to combine.

Second, Moniz claims a method for processing the noni plant into powder, and teaches that in the Caribbean *Morinda citrifolia* leaves are applied topically for aches and pains. It is inappropriate to rely on Moniz teaching that steamed leaves are topically applied in the Caribbean to relieve aches and pains because leaves are not fruit. Moniz does not suggest that the topical techniques of the Caribbean should be performed with the fruit, or that ingestion of the fruit would have the same affect as the topical leaf treatment. Additionally, Moniz in no way suggests utilizing noni in combination with a fruit extract to produce a food supplement as disclosed by Nair. It is not obvious that the same active ingredients present in leaves responsible for pain relief are present in fruit. Additionally, even if the fruit did contain the same active ingredient, there is no suggestion that that ingredient is a selective COX-2 inhibitor. Moniz does not suggest that the ameliorative effects of *Morinda citrifolia* are produced by COX-2 inhibition, let alone selective COX-2 inhibition.

In light of the absence of any suggestion or motivation to combine the above-referenced prior art, the mere fact that such prior art could be combined in the manner suggested by the Examiner does not render the present invention obvious. MPEP § 2142. Moreover, in this case the combined references fail to produce or suggest each element of the claimed invention.

To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, (CCPA 1974). Examiner admits that Moniz does not explicitly disclose the treatment of pain by the action of selective COX-2 inhibition, but argues that such a property is merely an inherent characteristic of *Morinda citrifolia*. Additionally, the Examiner relies on Nair, which disclose the use of fruit extracts to selectively inhibit COX-2 to treat inflammation and pain. The Examiner indicates that it would have been obvious to combine the teachings of Moniz and Nair. The Examiner then relies on the teachings of Wadsworth to teach the preparation of *Morinda citrifolia* products that are palatable but still retain their therapeutic qualities.

The treatment of pain by the action of selective COX-2 inhibition is not inherent in the prior art disclosures. Further, Specific COX-2 inhibition is not an inherent property of *Morinda citrifolia*. To establish inherency evidence “must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill...Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.” *Continental Can Co. v Monsanto Co.*, 948 F.2d 1264, 1268 (Fed. Cir. 1991).

The treatment of pain by the action of selective COX-2 inhibition is not inherent in the prior art disclosures. To be inherent the assumption must be made by the Examiner that because some fruit inhibit COX-2 and because Caribbean natives use *Morinda citrifolia* for aches and

pains, that *Morinda citrifolia* selectively inhibits COX-2. This is a leap in reasoning that could not be accepted by any reasonably scientific mind; “[i]nherency... may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.” *Continental Can Co. v Monsanto Co.*, 948 F.2d 1264, 1268 (Fed. Cir. 1991). It is not sufficient that it was, at the time of the present invention, a “probability or possibility” that *Morinda citrifolia* fruit, not leaves, would have the same ameliorative effects on aches and pains. Nor is it sufficient that there was a “probability or possibility” that the ameliorative effects of *Morinda citrifolia* fruit, if there were any, would be caused by selective inhibition of COX-2. Finally, it is not sufficient that there was a “probability or possibility” that selective COX-2 inhibition could be achieved with any particular dosage. Given the prior art references cited by the Examiner there was no more than a “probability or possibility” that a particular dosage of processed *Morinda citrifolia* product would selectively inhibit COX-2, and result in effective treatment for pain and inflammation. The mere fact that this discovery was made “from a given set of circumstances is not sufficient.” *Continental Can Co. v Monsanto Co.*, 948 F.2d 1264, 1268 (Fed. Cir. 1991). Thus selective COX-2 inhibition by the method of the present invention is not inherent in the prior art.

The treatment of pain by the action of selective COX-2 inhibition is not an inherent characteristic of *Morinda citrifolia*. Applicants claim “varying the concentration” of doses of *Morinda citrifolia* based on several factors in order to limit undesired COX-1 inhibition relative to COX-2 inhibition. *See Claims 1 and 12*. Applicants’ disclosure demonstrates the importance of administering the appropriate concentration of *Morinda citrifolia*. Their experiments demonstrate that at some concentrations selective COX-2 inhibition was achieved, and in other instances it was not. *See Specification, page 15*. The Applicants indicated that “the data suggests

the surprising result that in some circumstances ‘less’ *Morinda citrifolia* juice provides ‘more’ inhibition selectivity.” *Specification*, at 15.

Thus, the action of selective COX-2 inhibition is not inherent. If selective inhibition of COX-2 were an inherent characteristic of *Morinda citrifolia*, any concentration of *Morinda citrifolia* would result in the selective COX-2 inhibition because, as an inherent characteristic, it would be part of the “essential character” of *Morinda citrifolia*, not merely a probability or possibility that happened to occur from a given set of circumstances. *Continental Can Co. v Monsanto Co.*, 948 F.2d 1264, 1268 (Fed. Cir. 1991); *Merriam-Webster OnLine Dictionary* (2003). However, this is not the case; Applicants’ disclosure shows that COX-2 selectivity is undermined by excessive, increased concentrations. *See Specification, page 15*. It is only after the inherent COX-1 inhibiting qualities of *Morinda citrifolia* are limited by the methods of the present invention that selective COX-2 inhibition occurs.

Additionally, the Examiner has disregarded other significant claim elements in the present invention. For example, the prior art does not teach or suggest to specifically administer between 2 to 3 ounces of *Morinda citrifolia* two to three times daily for effective selective inhibition of COX-2. As stated by the Examiner, providing proper dosages is critical to providing effective and safe treatments (e.g., death can be caused by consuming too much vitamin A). Larger dosages are not always better, and decreased dosages are not always less effective. As such, the specific dosage included in the claims, as amended, function as the proper amount of *Morinda citrifolia* needed to effectively selectively inhibit COX-2. And, although this dosage may be varied, as stated in the claims depending upon the several factors, the dosage is limited to preferably be between 2 to 3 ounces. Since the combined prior art

references fail to teach or suggest all claim limitations of the present invention, Applicant submits that the present invention is not obvious. MPEP § 2143.

The Supreme Court in *Graham v. John Deere*, 383 U.S. 1, (1966), stated that “[u]nder § 103...[s]uch secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented. As indicia of obviousness or nonobviousness, these inquiries may have relevancy. . .” In *Stratoflex v. Aeroquip Corp.*, the secondary considerations were raised to the level of being a fourth *Graham* factor, “evidence rising out of the so-called ‘secondary considerations’ must always, when present, be considered en route to a determination of obviousness...evidence of secondary considerations may often be the most probative and cogent evidence on the record.” 713 F.2d 1530 (Fed. Cir. 1983). Selective inhibition of COX-2 is a long felt but unresolved need. If *Morinda citrifolia* had been obvious source of selective COX-2 inhibition someone skilled in the art the art would have utilized this information.

The Background for the Nair publication, cited against the present invention, provides a sufficient primer on the need to develop selective COX-2 inhibitors. The search for a selective COX inhibitor is more than a decade old. As a consequence of the monetary inducement to successfully produce a selective COX-2 inhibitor, it is clear that if the present invention had been obvious to one skilled in the art, and could have been accomplished with routine experimentation, that it would have been invented earlier by someone else. In fact, the present invention is surprising and non-obvious, as evidenced by the industries long felt and unresolved need to develop selective COX-2 inhibitors.

Applicant respectfully submits that Moniz in view of Nair and Wadsworth do not teach or suggest the limitations taught in claims 1-10, 12, and 13 discussed above. In particular because

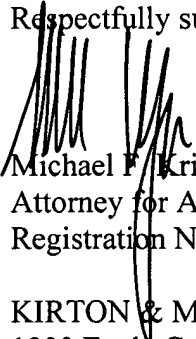
the Examiner failed to treat the claimed invention as a whole the Examiner reached the erroneous conclusion that the presently claimed method was borne from routine experimentation. The prior art does not suggest the combination of the prior art references cited against the present invention. All of the claim limitation of the present invention are not expressly taught in the prior art, and specific COX-2 inhibition is not an inherent property of *Morinda citrifolia*. Finally, selective inhibition of COX-2 is a long felt but unresolved need, which militates towards holding the present invention nonobvious. Accordingly, Applicant respectfully requests withdrawal of the Examiner's rejections under Section 103 (a) of claims 1-10, 12, and 13 as obvious over Moniz in view of Nair and Wadsworth.

CONCLUSION

Applicants submit that the claims are now in condition for allowance. Accordingly, Applicants request favorable reconsideration. If the Examiner has any questions or concerns regarding this communication, the Examiner is invited to call the undersigned.

DATED this 11 day of June, 2004.

Respectfully submitted,


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